UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

SECURITIES AND EXCHANGE COMMISSION,	:	
Plaintiff,	:	Civil Action No. 05-11805-NMG
v.	:	
RICHARD F. SELDEN,	:	
Defendant.	:	

NOTICE OF STATUS OF PROCEEDINGS IN THE DISTRICT OF COLUMBIA

In response to this Court's electronic notice of February 8, 2008, attached hereto as Exhibit A is the Stipulation And Order entered in the action captioned S.E.C. v. Selden, Misc. Case No. 1:05-mc-00476-RMU (D.D.C.) on February 27, 2008.

Dated: February 28, 2008
Boston, Massachusetts

Respectfully submitted,

/s/ Thomas J. Dougherty
Thomas J. Dougherty (BBO #132300)
SKADDEN, ARPS, SLATE,
MEAGHER & FLOM LLP
One Beacon Street
Boston, Massachusetts 02108
(617) 573-4800
dougherty@skadden.com

Counsel for Richard Selden

CERTIFICATE OF SERVICE

I, Thomas J. Dougherty, hereby certify that this document filed through the ECF system will be sent electronically to the registered participants as identified on the Notice of Electronic Filing (NEF) and paper copies will be sent to those indicated as non-registered participants on February 28, 2008.

Dated: February 28, 2008

/s/ Thomas J. Dougherty
Thomas J. Dougherty

EXHIBIT A

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

IN RE SUBPOENAS IN:

SECURITIES AND EXCHANGE COMMISSION,		
Plaintiff,	:	Miscellaneous Case No. 05-0476-RMU
v.	:	
RICHARD F. SELDEN,	:	(Related Case: Civ. No. 05-11805-NMG Pending in the United States District Court for the District of Massachusetts)
Defendant,	:	
and,	:	
FOOD AND DRUG ADMINISTRATION,	:	
Interested Party.	:	

STIPULATION AND ORDER

Based upon the following representation by the United States Food and Drug Administration ("FDA"), it is hereby stipulated and agreed that all pending motions in this action are hereby withdrawn:

The FDA hereby states that:

> The attached August 19, 2002 FDA Center for Biologics Evaluation And Research (CBER) letter's statement:
>
> > Replagal™ (agalsidase alfa) - An IND was submitted to FDA on November 1, 1996 for this product. The registration statement discussion on Replagal for long-term treatment of patients with Fabry disease is correct.
>
> addressed all aspects of the attached July 12, 2002 SEC letters' inquiries of FDA with respect to Replagal, including:
>
> > We would be interested in any comments regarding the accuracy of the information set forth in the registration statement. Also, please advise us of any facts or additional information which should be included in the registration statement to make the disclosure more meaningful to a potential investor.
>
> and:
>
> > Pursuant to regulations of the Food and Drug Administration, specifically 21 CFR 20.85 Disclosure to other Federal government departments and agencies, I hereby request the following records or information: The exact status of Replagal, Dynepo and Iduronate-2-sulfatase as described in the registration statement which may be currently under evaluation by the FDA.

SO ORDERED.

Ricardo M. Urbina
UNITED STATES DISTRICT JUDGE

Dated: February 27, 2008
Boston, Massachusetts

Respectfully submitted,

/s/ Marina Utgoff Braswell
JEFFREY A. TAYLOR,
D.C. BAR # 498610
United States Attorney

RUDOLPH CONTRERAS,
D.C. BAR # 434122
Assistant United States Attorney

MARINA UTGOFF BRASWELL
D.C. BAR # 416587
Assistant United States Attorney
U.S. Attorney's Office
555 4th Street, N.W. - Civil Division
Washington, D.C. 20530
(202) 514-7226

Counsel for
Food and Drug Administration

OF COUNSEL:

James C. Stansel
Acting General Counsel

Gerald F. Masoudi
Chief Counsel, Food and Drug Division

Eric M. Blumberg
Deputy Chief Counsel, Litigation

Jennifer Zachary
Assistant Chief Counsel
United States Department of
Health and Human Services
Office of General Counsel
5600 Fishers Lane
Rockville, Maryland 20857
(301) 827-9572

/s/ Joseph L. Barloon
Joseph L. Barloon (D.C. Bar No. 459626)
SKADDEN, ARPS, SLATE,
MEAGHER & FLOM LLP
1440 New York Avenue
Washington, D.C. 20005
(202) 371-7000

Thomas J. Dougherty
Justin J. Daniels
SKADDEN, ARPS, SLATE,
MEAGHER & FLOM LLP
One Beacon Street
Boston, Massachusetts 02108

Counsel for
Richard Selden

CERTIFICATE OF SERVICE

I, Joseph L. Barloon, hereby certify that this document filed through the ECF system will be sent electronically to the registered participants and that paper copies will be sent on February 27, 2008, to those indicated as non-registered participants, specifically:

Marina Utgoff Braswell
Laurie J. Weinstein
U.S. Attorney's Office
Judiciary Center Building
555 4th Street, N.W.
Washington, D.C. 20530

Jennifer L. Zachary
Assistant Chief Counsel
U.S. Department of Health & Human Services
Food and Drug Administration,
Office of the Chief Counsel
5600 Fishers Lane, GCF-1
Rockville, Maryland 20857

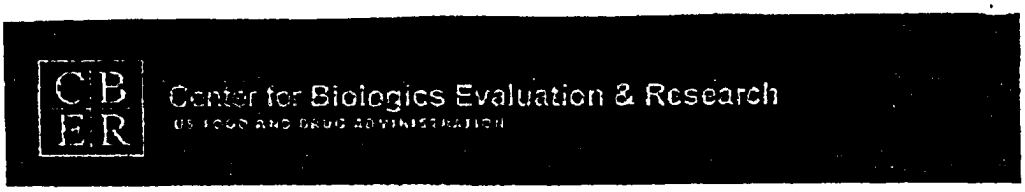
Frank Huntington
United States Securities and Exchange Commission
Boston District Office
33 Arch Street, 23rd Floor
Boston, Massachusetts 02110

Dated: February 27, 2008

/s/ Joseph L. Barloon
Joseph L. Barloon

ATTACHMENT 1

AUG-19-2002 14:53 FDA 301 827 6748 P.01



FDA FAX COVERSHEET

To:	Mr. Kevin Hands	**From:**	Juliaette Johnson
Fax:	(202) 942-9533	**Pages:**	2+ Coversheet
Phone:	(202) 942-2893	**Date:**	08/19/02
Re:	Commission File No. 333-90868	**CC:**	

☑ Urgent ☐ For Review ☐ Please Comment ☐ Please Reply ☐ Please Recycle

• Comments:

As per my telephone message to you on August 19, 2002, I am faxing a letter in reference to your CFR 20.85 request Re: Transkaryotic Therapies, Inc.
Registration Statement on Form S-3
Commission File No. 333-90868

Julia Johnson, R.N.

Tel: (301) 827-6355

Food & Drug Administration
Center for Biologics Evaluation and Research
Office of Compliance and biologics Quality
Division of Inspections and Surveillance (HFM-650)
1401 Rockville Pike, Suite 200S
Rockville, MD 20852-1448
FAX #: (301) 827-6748

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Center for Biologics Evaluation and Researc
1401 Rockville Pike
Rockville MD 20852-1448

August 19, 2002

Jeffrey P. Riedler, Assistant Director
Division of Corporate Finance
Securities and Exchange Commission
450 Fifth Street, NW
Washington, DC 20549

Re: Transkaryotic Therapies, Inc.
Registration Statement on Form S-3
Commission File No. 333-90868

Dear Mr. Riedler:

This is in response to your letter dated July 12, 2002, requesting agency review of registration statement filed by Transkaryotic Therapies Inc., with the SEC on June 20, 2002.
After a review of the Center for Biologics Evaluation and Research (CBER), the following information reflects the current status of the products outlined in the registration statement.

- Replagal™ (agalsidase alfa)- An IND was submitted to FDA on November 1, 1996 for this product. The registration statement discussion on Replagal for long-term treatment of patients with Fabry disease is correct.

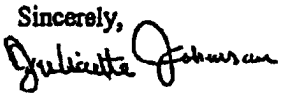
- Dynepo- The information referred to below the subheading ***Gene-Activated Protein Products***, on page 3, states a Phase III clinical trial assessing Dynepo as a treatment for anemia associated with cancer chemotherapy is ongoing; records could not be found listing this (it may be a non-US study). The registration statement correctly states on page 5, below the subheading ***Regulatory Risks***, that FDA refused to file the Biological License Agreement (BLA).

- Iduronate-2-sulfatase- An IND was submitted to FDA on December 21, 2000 for this product. Under this IND, the sponsor has completed a phase 1 study and has an ongoing study in which those subjects who completed the phase 1 study receive product. They are "planning" at least one subsequent study, which the sponsor generally refers to as a "phase 3" study in their communications. However, no substantive information on these plans has been submitted to CBER for review. Additionally, the data in the IND do not support the statement that treatment with I2S was generally "well tolerated by the 12 patients, and there is no data to verify the statements that the I2S " was clinically active" as referred to on page 3 below the subheading ***Transkaryotic Therapies, Inc.***

Please note that the information provided is not publicly disclosable without written permission from FDA CBER.

If I can be of further assistance, or answer any additional questions, you may contact me at (301) 827-6220. E-mail: johnsonju@cber.fda.gov.

Sincerely,



Juliaette Johnson, R.N.
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research

ATTACHMENT 2

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

DIVISION OF
CORPORATION FINANCE

July 12, 2002

Mail Stop 0309

Lana L. Ogram, Director
Division of Compliance Policy
C/o Anne Smith (HFC-230)
U.S. Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Re: Transkaryotic Therapies, Inc.
Registration Statement on Form S-3
Commission File No. 333-90868

Dear Ms. Smith:

Enclosed is a copy of the Registration Statement on Form S-3 filed with this Commission on June 20, 2002.

Since the company is subject to your Agency's review we would appreciate having the registration statement examined by your staff and receiving their comments, if any.

Although this Commission does not pass upon the merits of a security, it is concerned with compliance by a registrant with the statutory requirements of fair and accurate disclosure of information to public investors. We would be interested in any comments regarding the accuracy of the information set forth in the registration statement. Also, please advise us of any facts or additional information which should be included in the registration statement to make the disclosure more meaningful to a potential investor.

We anticipate completing our review of this company's registration statement in the near future and we would appreciate any comments as soon as possible.

If you have any questions with regard to this matter, please call Kevin Hands at (202) 942-2893.

Sincerely,

for Jeffrey P. Riedler
Assistant Director

Date: July 12, 2002

TO: Associate Commissioner for Regulatory Affairs (HFC-1)
Food and Drug Administration
5600 Fisher Lane
Rockville, MD 20857

Re: Transkaryotic Therapies, Inc.
SEC File No. 333-90868

Pursuant to regulations of the Food and Drug Administration, specifically 21 CFR 20.85 Disclosure to other Federal government departments and agencies, I hereby request the following records or information: The exact status of Replagal, Dynepo and Iduronate-2-sulfatase as described in the registration statement which may be currently under evaluation by the FDA.

I understand that 21 USC 331 (j) prohibits the disclosure of trade secrets outside the Department of Health and Human Services.

I certify that the records or information will be used for the following law enforcement activity: To assure that disclosure in the registration statement by the registrant is correct and complete. Disclosure of the information will be made only to the registrant.

I further certify that this law enforcement activity is authorized by law, that the records or information will be used only for the stated purposes and will not be further disclosed without the written permission of the Food and Drug Administration.

Signed: KPH _____

for Jeffrey P. Riedler

Title: Assistant Director, Division of Corporation Finance

Agency: Securities and Exchange Commission

In view of the time constraints under which the staff is operating, it would be appreciated if you would fax any information to the attention of Kevin Hands at the fax number (202) 942-9533.

FDA OCC 827

As filed with the Securities and Exchange Commission on June 20, 2002
Registration Statement No. 333-

SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM S-3
REGISTRATION STATEMENT UNDER THE SECURITIES ACT OF 1933

TRANSKARYOTIC THERAPIES, INC.
(Exact name of registrant as specified in its charter)

Delaware	04-3027191
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification Number)

195 Albany Street
Cambridge, Massachusetts 02139
(617) 349-0200
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Richard F Selden, M.D., Ph.D.
President and Chief Executive Officer
Transkaryotic Therapies, Inc.
195 Albany Street
Cambridge, Massachusetts 02139
(617) 349-0200
(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

Michael J. Astrue, Esq.	David E. Redlick, Esq.
Transkaryotic Therapies, Inc.	Hale and Dorr LLP
195 Albany Street	60 State Street
Cambridge, Massachusetts 02139	Boston, Massachusetts 02109
(617) 349-0200	(617) 526-6000

Approximate date of commencement of proposed sale to public: As soon as practicable after this Registration Statement becomes effective.

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box. ☐

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box. ☒

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐ _____

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐ _____

If delivery of the prospectus is expected to be made pursuant to Rule 434, please check the following box. ☐

CALCULATION OF REGISTRATION FEE

Title of Shares to be Registered	Amount to be Registered	Proposed Maximum Offering Price Per Share(1)	Proposed Maximum Aggregate Offering Price(1)	Amount of Registration Fee
Common Stock, $0.01 par value per share (including associated preferred stock purchase rights)	366,928	$33.49	$12,288,419	$1,131

(1) Estimated solely for purposes of calculating the registration fee pursuant to Rule 457(c) under the Securities Act and based upon the average of the high and low prices reported on The Nasdaq National Market on June 14, 2002.

The Company hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Company shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the Registration Statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), shall determine.

Subject to completion, dated June 20, 2002

PROSPECTUS

[TKT LOGO HERE]

TRANSKARYOTIC THERAPIES, INC

366,928 SHARES OF COMMON STOCK

This prospectus relates to resales of up to 366,928 shares of common stock of Transkaryotic Therapies, Inc., which we issued to Cell Genesys, Inc. as partial payment for an exclusive license to intellectual property owned by Cell Genesys.

We will not receive any proceeds from sales of the shares of common stock offered by this prospectus.

Cell Genesys, which we refer to in this prospectus as the selling stockholder, or its pledgees, donees, transferees or other successors-in-interest, may offer the shares from time to time through public or private transactions at prevailing market prices, at prices related to prevailing market prices or at privately negotiated prices.

Our common stock is listed on The Nasdaq National Market under the symbol "TKTX." The last reported sale price of our common stock on June 19, 2002 was $36.26 per share. We urge you to obtain current market quotations for our common stock.

Investing in our common stock involves a high degree of risk. See "Risk Factors" beginning on page 5.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is , 2002.

TABLE OF CONTENTS

We have not authorized anyone to provide you with information different from that contained or incorporated by reference in this prospectus. The selling stockholder is offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or of any sale of common stock.

PROSPECTUS SUMMARY

This summary highlights important features of this offering and the information included or incorporated by reference in this prospectus. This summary does not contain all of the information that you should consider before investing in our common stock. You should read the entire prospectus carefully, especially the risks of investing in our common stock discussed under "Risk Factors."

Transkaryotic Therapies, Inc.

We are a biopharmaceutical company developing protein- and cell-based therapeutics for the treatment of a wide range of human diseases. During 2001, we received our first marketing approvals. We are building a broad and renewable product pipeline based on three proprietary development platforms: Niche Protein® products, Gene-Activated® proteins and Transkaryotic Therapy™ gene therapy products.

Replagal™ (agalsidase alfa), our enzyme replacement therapy for the long-term treatment of patients with Fabry disease, was granted marketing authorization in the European Union in August 2001. We have also received approval to market Replagal in Australia, The Czech Republic, Iceland, Israel, New Zealand, Norway, and Switzerland. In September 2001, we launched Replagal in Europe. We recorded $3.5 million in product sales in 2001, and $6.1 million in product sales in the first quarter of 2002.

We have additional products currently undergoing human clinical testing, including:

Niche Protein Products:

- Iduronate-2-sulfatase, or I2S, our investigational enzyme replacement therapy for the treatment of Hunter syndrome, has completed a Phase I/II trial. Preliminary results from the trial indicate that treatment with I2S was generally well-tolerated by the 12 patients participating in the trial and that I2S was clinically active in these patients. Based on these results, we intend to conduct a pivotal Phase III study of I2S.

Gene-Activated Protein Products:

- Dynepo™, a Gene-Activated erythropoietin for the treatment of anemia related to chronic renal failure, has completed Phase III studies. In March 2002, the European Commission, or EC, granted marketing approval of Dynepo in the European Union. We and our partner, Aventis Pharma, also are currently seeking marketing approval of Dynepo in the United States. The launch of Dynepo has not been planned due to ongoing litigation. In addition, a Phase III clinical trial assessing Dynepo as a treatment for anemia associated with cancer chemotherapy is ongoing.

Gene Therapy:

- Factor VIII Transkaryotic Therapy, a gene therapy product to treat patients with hemophilia A, has completed a Phase I clinical trial.

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below before purchasing our common stock. The risks and uncertainties described below are not the only ones facing our company. Additional risks and uncertainties may also impair our business operations. If any of the following risks actually occur, our business, financial condition or results of operations would likely suffer. In that case, the trading price of our common stock could fall, and you could lose all or part of the money you paid to buy our common stock.

Regulatory Risks

We may not be able to obtain marketing approvals for our products.

We are not able to market any of our products in Europe, the United States or in any other jurisdiction without marketing approval from the European Agency for the Evaluation of Medicinal Products, or EMEA, the United States Food and Drug Administration, or FDA, or any equivalent foreign regulatory agency. The regulatory process to obtain market approval for a new drug or biologic takes many years and requires the expenditure of substantial resources. We have had only limited experience in preparing applications and obtaining regulatory approvals.

Replagal was granted marketing authorization in the fifteen countries of the European Union by the European Commission in August 2001. We have also received approval to market Replagal in Australia, The Czech Republic, Iceland, Israel, New Zealand, Norway, and Switzerland.

In the United States, we submitted a Biologics License Application, or BLA, to the FDA seeking marketing authorization for Replagal. In January 2001, the FDA issued a complete review letter regarding the BLA for Replagal. The FDA letter stated that the data that we had provided was not adequate for approval of the BLA at that time and requested additional information. In response to this letter, we have discussed the BLA with the FDA and have submitted additional data. We expect that after the FDA has reviewed the data, it will either approve the BLA or decline to approve it. If it declines to approve the BLA, the FDA may request additional information, possibly including data from additional clinical trials.

During 2000, Aventis submitted a Marketing Authorization Application, or MAA, to the EMEA seeking marketing authorization of Dynepo in the European Union for the treatment of anemia associated with kidney disease. In March 2002, the EC granted marketing approval of Dynepo in the European Union.

Also during 2000, Aventis submitted a BLA to the FDA seeking marketing authorization for Dynepo in the United States. The FDA did not accept this BLA for filing, requesting that Aventis provide additional manufacturing data. Aventis is currently accumulating these data and, when complete, we expect that Aventis will submit a new BLA.

There can be no assurance as to whether or when any of these applications for marketing authorization relating to Replagal and Dynepo, or additional applications for marketing authorization that we may make in the future as to these or other products, will be approved by the relevant regulatory authorities.

If we fail to comply with the extensive regulatory requirements to which our products are subject, we could be subject to adverse consequences and penalties.

The testing, manufacturing, labeling, advertising, promotion, export, and marketing, among other things, of our products are subject to extensive regulation by governmental authorities in Europe, the United States, and elsewhere throughout the world.

In general, there can be no assurance that submission of materials requesting permission to conduct clinical trials will result in authorization by the EMEA, the FDA or equivalent foreign regulatory agency to commence clinical trials, or that once clinical trials have begun, testing will be completed successfully within any specific time period, if at all, with respect to any of our products. Once trials are complete and an application has been submitted to the relevant regulatory agency, the regulatory agency may deny the application if applicable regulatory criteria are not satisfied, or may require additional testing or information.

If regulatory approval of a product is granted, such approval may be subject to limitations on the indicated uses for which the product may be marketed or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the product. As to any product for which we obtain marketing approval, the product, the facilities at which the product is manufactured, any post-approval clinical data and our promotional activities will be subject to continual review and periodic inspections by the EMEA, the FDA and other regulatory authorities.

Both before and after approval is obtained, violations of regulatory requirements may result in various adverse consequences, including the EMEA's or FDA's delay in approving or refusal to approve a product, suspension or withdrawal of an approved product from the market, operating restrictions, or the imposition of civil or criminal penalties.

We may not be able to obtain orphan drug exclusivity for our Niche Protein products. If our competitors are able to obtain orphan drug exclusivity before us, we may be precluded from marketing our Niche Protein products.

Some jurisdictions, including Europe and the United States, may designate drugs for relatively small patient populations as "orphan drugs." Generally, if a product which has an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to orphan drug exclusivity. Orphan drug exclusivity means that applications to market the same product for the same use may not be approved, except in very limited circumstances, for a period of up to 10 years in Europe and for a period of seven years in the United States. Obtaining orphan drug designations and orphan drug exclusivity for our Niche Protein products may be critical to the success of this platform. Even if we obtain orphan drug exclusivity for any of our potential products, we may not be able to maintain it. For example, if a competitive product is shown to be clinically superior to our product, any orphan drug exclusivity we have obtained will not apply to such competitive product. Our competitors may also seek and obtain orphan drug exclusivity for products competitive with our products before we obtain marketing approval.

Replagal was granted marketing authorization in the fifteen countries of the European Union by the European Commission in August 2001. A competitive product for the treatment of patients with Fabry disease, marketed by Genzyme Corporation, was also granted marketing authorization in the European Union. Both Replagal and Genzyme's competing product were granted co-exclusive orphan drug status in the European Union for up to 10 years.

In the United States, both we and Genzyme have received orphan drug designation for our respective products for Fabry disease. Whichever product is the first to receive FDA marketing approval would likely receive orphan drug exclusivity for that product. Once a product receives orphan drug exclusivity, the FDA may not approve any other applications to market the same class of product for Fabry disease for a period of seven years, except in limited circumstances.

If our clinical trials are not successful, we may not be able to develop and commercialize our products.

In order to obtain regulatory approvals for the commercial sale of our potential products, we and our collaborators will be required to complete extensive clinical trials in humans to demonstrate the

safety and efficacy of our products. We may not be able to obtain authority from the EMEA, the FDA or other regulatory agencies to commence or complete these clinical trials.

The results from preclinical testing of a product that is under development may not be predictive of results that will be obtained in human clinical trials. In addition, the results of early human clinical trials may not be predictive of results that will be obtained in larger scale, advanced stage clinical trials. Furthermore, we, one of our collaborators, or a regulatory agency with jurisdiction over the trials may suspend clinical trials at any time if the subjects or patients participating in such trials are being exposed to unacceptable health risks, or for other reasons.

The rate of completion of clinical trials is dependent in part upon the rate of enrollment of patients. Patient accrual is a function of many factors, including the size of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the study, the existence of competitive clinical trials, and the availability of alternative treatments. In particular, the patient populations for some of our Niche Protein products are small. Delays in planned patient enrollment may result in increased costs and prolonged clinical development.

We and our collaborators may not be able to successfully complete any clinical trial of a potential product within any specified time period. In some cases, we may not be able to complete the trial at all. Moreover, clinical trials may not show our potential product to be both safe and efficacious. Thus, the EMEA, the FDA and other regulatory authorities may not approve any of our potential products for any indication.

Because gene therapy is a relatively new technology and gene therapy products have not been extensively tested in humans, we may face delays and incur increased costs in the regulatory process related to our gene therapy products.

We are developing gene therapy products. Because gene therapy is a relatively new technology and products for gene therapy have not been extensively tested in humans, the regulatory requirements governing gene therapy products may be more uncertain than for other types of products. This uncertainty may cause delays in the regulatory process relating to our gene therapy products, including delays in our initiating clinical trials of these products. This uncertainty may also increase the cost of obtaining regulatory approvals of our gene therapy products.

Ethical and social issues may cause regulatory authorities to increase the regulation of gene therapy clinical trials.

Due to adverse events that have occurred during some gene therapy clinical trials conducted by other biotechnology and pharmaceutical companies and institutions, the Federal government, the EMEA, the FDA, industry organizations, and institutions conducting gene therapy clinical trials have grown increasingly concerned about the safety of these clinical trials. An increased concern over gene therapy trials generally may lead the EMEA, the FDA or other regulatory agencies to impose further regulation on gene therapy clinical trials. If further regulations are imposed on gene therapy research generally, the delays and costs involved in complying with such regulations may impair our ability to conduct gene therapy clinical trials in the future.

Patent Litigation and Intellectual Property Risks

We are a party to litigation with Genzyme and Mount Sinai involving Replagal which could preclude us from manufacturing or selling Replagal.

Since July 2000, we have been involved in patent litigation relating to Replagal brought by Genzyme and Mount Sinai School of Medicine in the U.S. District Court for the District of Delaware regarding a patent licensed by Genzyme from Mount Sinai. In January 2002, the Delaware District

Court dismissed this patent litigation, granting our motion for summary judgment of non-infringement and denying Genzyme's motion for summary judgment of infringement. In March 2002, Genzyme appealed the ruling of the Delaware District Court to the U.S. Federal Circuit Court of Appeals. If Genzyme is successful in its appeal, we may be precluded from marketing and selling Replagal. We can provide no assurance as to the outcome of this litigation.

We are a party to litigation with Amgen and Kirin-Amgen involving Dynepo which could preclude us from manufacturing or selling Dynepo.

In April 1997, Amgen, Inc. commenced a patent infringement action against us and Aventis in the U.S. District Court for the District of Massachusetts. In January 2001, the Massachusetts District Court concluded that Dynepo infringed 8 of the 18 claims of patents asserted by Amgen. Amgen did not seek and was not awarded monetary damages. We and Aventis have filed an appeal of the decision with the U.S. Federal Circuit Court of Appeals. Amgen has also appealed this decision.

In addition, in July 1999, we and Aventis commenced legal proceedings in the U.K. against Kirin-Amgen, Inc., seeking a declaration that a U.K. patent held by Kirin-Amgen will not be infringed by our activities related to Dynepo and that certain claims of Kirin-Amgen's U.K. patent are invalid. In April 2001, the High Court of Justice in the United Kingdom ruled that Dynepo infringed one of four claims of a patent asserted by Kirin-Amgen. We and Aventis have filed an appeal of this decision. Kirin-Amgen has also appealed this decision.

We can provide no assurance as to the outcome of either litigation. Unless we and Aventis are successful in our appeals, we and Aventis will be precluded from manufacturing and selling Dynepo in the relevant jurisdictions. In addition, the launch of Dynepo has not been planned due to this litigation. The litigation is costly and we are required to reimburse Aventis, which is paying the litigation expenses, for our share of the expenses from future royalties and in other circumstances.

We may become involved in additional and expensive patent litigation or other proceedings.

The biotechnology industry has been characterized by significant litigation, and interference and other proceedings regarding patents, patent applications, and other intellectual property rights. We may become a party to additional patent litigation and other proceedings with respect to our Niche Protein products, Gene-Activated proteins, Transkaryotic gene therapy technology or other technologies. Such litigation could result in liability for damages, prevent our development and commercialization efforts, and divert management's attention and resources.

An adverse outcome in any patent litigation or other proceeding involving patents could subject us to significant liabilities to third parties and require us to cease using the technology or product that is at issue or to license the technology or product from third parties. We may not be able to obtain any required licenses on commercially acceptable terms, or at all.

The cost to us of any patent litigation or other proceeding, even if resolved in our favor, could be substantial. Some of our competitors may be able to sustain these costs more effectively than we can because of their substantially greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to develop, manufacture, and market products, form strategic alliances, and compete in the marketplace.

If we are unable to obtain patent protection for our discoveries, the value of our technology and products may be adversely affected.

Our success will depend in large part on our ability to obtain patent protection for our processes and products in the United States and other countries. The patent situation in the field of

biotechnology generally is highly uncertain and involves complex legal, scientific and factual questions. We may not be issued patents relating to our technology. Even if issued, patents may be challenged, invalidated, or circumvented. Our patents also may not afford us protection against competitors with similar technology. Because patent applications in the United States are maintained in secrecy until patents issue, third parties may have filed or maintained patent applications for technology used by us or covered by our pending patent applications without our being aware of these applications.

We may not hold proprietary rights to certain product patents, process patents, and use patents related to our products or their methods of manufacture. In some cases, these patents may be owned or controlled by third parties. As a result, we may be required to obtain licenses under third party patents to market certain of our potential products. If licenses are not available to us on acceptable terms, we may not be able to market these products.

If we are unable to protect the confidentiality of our proprietary information and know-how, the value of our technology and products will be adversely affected.

We rely upon unpatented proprietary technology, processes, and know-how. We seek to protect this information in part by confidentiality agreements with our employees, consultants, and other third party contractors. These agreements may be breached, and we may not have adequate remedies for any such breach. In addition, our trade secrets may otherwise become known or be independently developed by competitors.

If we fail to comply with any of our obligations under any of the agreements under which we license commercialization rights to products or technology from third parties, we could lose license rights that are important to our business.

We are a party to a number of patent licenses that are important to our business and expect to enter into additional patent licenses in the future. These licenses impose various commercialization, sublicensing, royalty, insurance, and other obligations on us. If we fail to comply with these obligations, the licensor may have the right to terminate the license and we may not be able to market products that were covered by the license.

Business Risks

Our revenue from product sales is dependent on the commercial success of Replagal

During 2001, we received marketing authorizations for our first product. Replagal was granted marketing authorization in the European Union in August 2001. We have also received approval to market Replagal in seven other countries. We expect that Replagal will account for all of our product sales into 2004, at the earliest. The commercial success of Replagal will depend on its acceptance by physicians, patients and other key decision-makers for the treatment of Fabry disease. If Replagal does not generate significant product sales, we will be required to fund operations with cash resources, interest income, proceeds from equity offerings and debt financings and funding from collaborative agreements.

The market may not be receptive to our products upon their introduction.

The commercial success of any of our products for which we obtain marketing approval from the EMEA, the FDA, and other regulatory authorities will depend upon their acceptance by patients, the medical community and third party payors as clinically effective, safe and cost-effective. It may be difficult for us to achieve market acceptance of our products.

Other factors that we believe will materially affect market acceptance of our products include:

- the timing of the receipt of marketing approvals;
- the countries in which such approvals are obtained; and
- the safety, efficacy, convenience, and cost-effectiveness of the product as compared to competitive products.

We have limited experience and resources in manufacturing and will incur significant costs to develop this experience or rely on third parties to manufacture our products on our behalf.

We have limited manufacturing experience and in order to continue to develop products, apply for regulatory approvals, and commercialize our products, we will need to develop, contract for, or otherwise arrange for the necessary manufacturing capabilities. We currently use, and expect to continue to use in the future, internal manufacturing and contract manufacturing by third parties to meet our production requirements for preclinical testing, clinical trials, and commercial supply.

To the extent that we are a party to manufacturing arrangements with third parties, we will be dependent upon these third parties to perform their obligations in a timely manner and in accordance with applicable government regulations. There are a limited number of such third-party manufacturers capable of manufacturing our protein products with a limited amount of production capacity. As a result, we may experience difficulty in obtaining adequate manufacturing capacity for our needs. If we are unable to obtain or maintain contract manufacturing of these products, or to do so on commercially reasonable terms, we may not be able to complete development of these products or market them.

To the extent that we elect not to or cannot contract for third-party manufacturing for any of our products, we will need to manufacture these products in our own manufacturing facilities. We have limited manufacturing experience. We are investing, and may need to invest in the future, substantial additional funds to build our own manufacturing facilities and need to recruit qualified personnel in order to build or lease and operate any manufacturing facilities. There can be no assurance that we will be able to successfully build or operate our own facilities, that our facilities will comply with applicable regulations or that our facilities will enable us to manufacture our products at a commercially reasonable cost.

If we fail to obtain an adequate level of reimbursement by third party payors for our products, we may not have commercially viable markets for our products.

In certain countries, particularly the countries of the European Union, the pricing of prescription pharmaceuticals and the level of reimbursement are subject to governmental control. In the United States, the availability of reimbursement by governmental and other third party payors affects the market for any pharmaceutical product. These third party payors continually attempt to contain or reduce the costs of health care by challenging the prices charged for medical products and services.

We expect that the prices for many of our products, when commercialized, including in particular, our Niche Protein products, may be high compared to other pharmaceutical products. We have established pricing and reimbursement in substantially all countries in Europe in which Replagal has been approved. The average price established is approximately $165,000 per patient per year. We have not established reimbursement for Replagal in all of the countries in which it has been approved and may not establish reimbursement in one or more of those countries at adequate levels or at all. The price of our products may make reimbursement more difficult to obtain, if it can be obtained at all.

The Centers for Medicare and Medicaid Services of the United States Department of Health and Human Services has considered proposals from time to time to reduce the reimbursement rate with respect to erythropoietin. If Dynepo is approved and commercialized, adoption by the Centers for

Medicare and Medicaid Services of any such proposal might have an adverse effect on the pricing of Dynepo.

We also may experience pricing pressure with respect to Replagal and other products for which we may obtain marketing approval due to the trend toward managed health care, the increasing influence of health maintenance organizations and legislative proposals. We may not be able to sell our products profitably if reimbursement is unavailable or limited in scope or amount.

We face significant competition, which may result in others discovering, developing or commercializing products before, or more successfully, than we do.

The biotechnology industry is highly competitive and characterized by rapid and significant technological change. Our competitors include pharmaceutical companies, biotechnology firms, universities, and other research institutions. Many of these competitors have substantially greater financial and other resources than we do and are conducting extensive research and development activities on technologies and products similar to, or competitive, with ours.

We may be unable to develop technologies and products that are more clinically efficacious or cost-effective than products developed by our competitors. Even if we obtain marketing approval for our product candidates, many of our competitors have more extensive and established sales, marketing, and distribution capabilities than we do. Litigation with third parties, including litigation with Amgen and Genzyme, could delay our time to market or preclude us from reaching the market for certain products and enable our competitors to more quickly and effectively penetrate certain markets.

Niche Protein Products. For many of the disease targets of our Niche Protein product platform, there is currently no cure or effective treatment. Treatments generally are focused on the management of the disease's symptoms. In general, we believe that these diseases represent markets too small to attract the resources of larger pharmaceutical companies but may provide attractive commercial opportunities to smaller companies.

We believe that the primary competition with respect to our Niche Protein product program is from biotechnology and smaller pharmaceutical companies. Competitors include BioMarin Pharmaceutical Inc., Genzyme, and Oxford GlycoSciences plc. The markets for some of the potential Niche Protein products are quite small. As a result, if competitive products exist, we may not be able to successfully commercialize our products.

We believe that our primary competition with respect to Replagal is Genzyme. Replagal was granted marketing authorization in the fifteen countries of the European Union by the European Commission in August 2001. A competitive product for the treatment of patients with Fabry disease, marketed by Genzyme, was also granted marketing authorization in the European Union. Both Replagal and Genzyme's competing product were granted co-exclusive orphan drug status in the European Union for up to 10 years.

In the United States, both we and Genzyme have received orphan drug designation for our respective products for Fabry disease. Whichever product is the first to receive FDA marketing approval would likely receive orphan drug exclusivity for that product. Once a product receives orphan drug exclusivity, the FDA may not approve any other applications to market the same class of product for Fabry disease for a period of seven years, except in limited circumstances.

Gene-Activated Protein Products. In our Gene-Activated protein program, we are developing potentially improved versions of proteins that are currently marketed and proteins that have no currently-marketed counterparts. For instance, in the case of Dynepo, erythropoietin and competing products are marketed by Amgen, Johnson & Johnson, F. Hoffmann-La Roche Ltd. (Boehringer Mannheim GmbH), Sankyo Company Ltd., Chugai Pharmaceutical Co., Ltd., and the pharmaceutical division of Kirin Brewery Co., Ltd.

Many of the protein products against which our Gene-Activated proteins would compete have well-known brand names, have been promoted extensively and have achieved market acceptance by third-party payors, hospitals, physicians, and patients. In addition, many of the companies that produce these protein products have patents covering techniques used to produce these products, which have served as effective barriers to entry in the therapeutic proteins market. As with Amgen and its erythropoietin product, these companies may seek to block our entry into the market by asserting that our Gene-Activated proteins infringe their patents. Many of these companies are also seeking to develop and commercialize new or potentially improved versions of their proteins

Gene Therapy. Our gene therapy system will have to compete with other gene therapy systems, as well as with conventional methods of treating the diseases and conditions targeted. Although no gene therapy product is currently marketed in the United States, a number of companies, including major biotechnology and pharmaceutical companies, as well as development stage companies, are actively involved in this field.

Competition for technical, commercial and administrative personnel is intense in our industry and we may not be able to sustain our operations or grow if we are unable to attract and retain key personnel.

Our success is highly dependent on the retention of principal members of our technical, commercial, and administrative staff. Furthermore, our future growth will require hiring a significant number of qualified technical, commercial and administrative personnel. Accordingly, recruiting and retaining such personnel in the future will be critical to our success. There is intense competition from other companies and research and academic institutions for qualified personnel in the areas of our activities. If we are not able to continue to attract and retain, on acceptable terms, the qualified personnel necessary for the continued development of our business, we may not be able to sustain our operations or grow.

We have limited sales and marketing experience and capabilities and will need to develop this expertise or depend on third parties to successfully sell and market our products on our behalf.

We have limited sales and marketing experience and capabilities. In order to market our products, including Replagal, we will need to develop this experience and these capabilities or rely upon third parties, such as our collaborators, to perform these functions. If we rely on third parties to sell, market, or distribute our products, our success will be dependent upon the efforts of these third parties in performing these functions. In many instances, we may have little or no control over the activities of these third parties in selling, marketing, and distributing our products. If we choose to conduct these activities directly, as we plan to do with respect to some of our potential products, we may not be able to recruit and maintain an effective sales force.

We depend on our collaborators to develop, conduct clinical trials, obtain regulatory approvals for, and manufacture, market and sell certain products on our behalf and none of their efforts may be scientifically or commercially successful.

We are parties to collaborative agreements with third parties relating to certain of our principal products. We are relying on Aventis to develop, conduct clinical trials, obtain regulatory approvals for, and manufacture, market, and sell Dynepo in the United States and Europe; Sumitomo Pharmaceuticals Co., Ltd. to develop and commercialize Replagal for Fabry disease in Japan and other Asian countries; and Genetics Institute, Inc. to co-develop and commercialize Factor VIII gene therapy for hemophilia A in Europe. Our collaborators may not devote the resources necessary or may otherwise be unable or unwilling to complete development and commercialization of these potential products. Our existing collaborations are subject to termination without cause on short notice under specified circumstances.